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EXAMINER	
VIVLEMORE, TRACY ANN	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 09/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/028,415	LASHAM ET AL.	
	Examiner	Art Unit	
	Tracy Vivlemore	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 9-24* is/are pending in the application.

4a) Of the above claim(s) *1-5,12,13 and 17-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6, 9-11, 14-16 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/13/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group II, claims 6-11 and 14-16 in the reply filed on July 16, 2004 is acknowledged.

Applicant has canceled claims 7 and 8 and added new claim 24, which is drawn to the elected invention. With this amendment, claims 1-6 and 9-24 are pending.

Claims 1-5, 12, 13, and 17-23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on July 16, 2004.

Priority

Human Y-box 1 and the cold shock domain of human YB-1 as described in SEQ ID NOS: 39 and 40 as well as methods of modulating apoptosis by reducing the amount of a transcriptional regulator of apoptosis are not supported by the disclosure of application 08/713,557, now issued as US patent 5,912,168. Thus, the earliest date of priority to which these aspects of the instant application is entitled is the filing date of application 09/036,004, March 4, 1998. If applicant believes that support is to be found in US patent 5,912,168 for these sequences and methods, applicant is requested in reply to this action to point out, with particularity, where such support can be found.

Acknowledgment is made of applicant's claim for foreign priority based on an application filed with the international bureau on November 28, 2001. It is noted,

however, that applicant has not filed a certified copy of the PCT/NZ01/00286 application as required by 35 U.S.C. 119(b).

Specification

The disclosure is objected to because of the following informalities: the cross-reference to related applications should recite the status of each application. There is no disclosure of the current status of application number 09/724,809.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6, 9-11, 14-16 and 24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

1. Claims 6-11, 14-16 and 24 are drawn to methods of increasing apoptotic cell death in a population of cells by reducing the amount of a transcriptional regulator of apoptosis (hereafter referred to as TRA) available to bind to a target polynucleotide. The TRA is defined to be the human Y-box 1 protein (YB-1), the cold shock domain of

this protein and sequences having 75% or more identity to these two proteins. Additional limitations recited include the use of the claimed method to increase apoptotic cell death in tumor cells, the use of antisense or decoy oligonucleotides to reduce the amount of the TRA available to bind the target polynucleotide and the use of the claimed method to increase expression of p53. The methods as claimed encompass use *ex vivo* in cell culture and *in vivo* in all organisms. The methods as claimed also encompass use of the method to treat disease, as evidenced by claim 10, which is drawn to the use of the claimed method in tumor cells.

2. The specification teaches on page 1-2 that regulation of apoptosis has important therapeutic applications against diseases such as Alzheimer's, Parkinson's and multiple sclerosis; ischemic conditions such as heart attack and stroke and even against viral infections such as HIV. Delivery methods for therapeutic nucleic acids are contemplated on pages 14 and 15. The specification teaches in example 2 (pages 26-29) use of ten antisense and two decoy oligonucleotide sequences to modulate the binding of YB-1 and Pur-α to the CD95 promoter and thus modulate apoptosis in HepG2 (liver carcinoma) cells. In example 4 (pages 30-33) the disclosed antisense and decoy oligonucleotides of YB-1 were also shown to modulate apoptosis by activating p53 in several human cancer cell lines. Example 3 (page 30) describes one *in vivo* use of antisense and decoy oligonucleotides targeted against YB-1 to modulate apoptosis in mice.

3. The methods as claimed encompass antisense oligonucleotides against YB-1, the cold shock domain of this protein and sequences having greater than 75% identity

to one of these sequences. The encompassed antisense sequences constitute a large genus of antisense compounds. The instant specification discloses ten sequences (described in example 2) described as being antisense to YB-1, which are not representative of the claimed genus. The specification describes these antisense sequences on pages 12-13 as "exemplary". The specification also states that antisense sequences should be sufficiently complementary to the polynucleotide encoding a TRA to bind specifically but complementarity need not be 100%. The specification does not give any guidance as to the desired size of an antisense oligonucleotide, what region of YB-1 the antisense should be complementary to or any defining characteristics beyond complementarity. Branch (TIBS 1998, vol. 23, p. 45-50) describes on page 49, in the paragraph bridging columns 1 and 2, that "Because it is very difficult to predict what portions of an RNA molecule will be accessible *in vivo,* effective antisense molecules must be found empirically by screening a large number of candidates for their ability to act inside cells" and that in one report of screening antisense sequences it was found that "only 3% of the antisense molecules tested in this system were highly effective; 40% had almost no effect." There is no guidance in the specification describing the desired structure of a decoy oligonucleotide such as minimum or maximum size or the presence or absence of sugar or backbone modifications. The structure of the target has not been described, it is impossible to envision the structure of the antisense or decoy sequences that will bind to the target.

4. The claimed methods encompass antisense sequences that are complementary to sequences having at least 75% identity to either YB-1 or its cold shock domain. Thus

sequences that are up to 25% non-identical to YB-1 or its cold shock domain and all antisense sequences to *all* portions of said sequences, including antisense sequences that may have no complementarity to YB-1 or its cold shock domain, are included within the instant claims. The specification provides no description of antisense sequences complementary to the portion of a sequence that has no identity with YB-1 or its cold shock domain and provides no description of how such sequences with no identity to YB-1 or its cold shock domain would be used to modulate apoptosis by the claimed method.

5. Thus, the specification provides description of ten antisense oligonucleotide targeted to YB-1, but does not provide adequate written description of the entire genus of oligonucleotides capable of modulating apoptosis by binding to YB-1, the cold shock domain of this protein and sequences having 75% or more identity to these two proteins including the antisense oligonucleotides that are complementary to the 25% of a sequence that is not complementary to YB-1 or its cold shock domain.

6. The specification lacks adequate description of the structure of antisense molecules to YB-1 or its cold shock domain that would be effective in modulating apoptosis, including the oligonucleotides complementary to regions of sequences having no complementarity to YB-1 or its cold shock domain, how to administer them to any organism in an appropriate dose and how to deliver the antisense sequence in a manner so as to effect a modulation of apoptosis in a particular tissue or cell. The examples described in the specification describe several antisense sequences delivered to modulate apoptosis in mice. No experiments were done with antisense sequences

delivered to any organism in order to treat disease other than fibrosarcoma in mice. There is no description that would show the skilled artisan how to treat any other disease in any other organism using antisense to YB-1 or its cold shock domain or antisense sequences that are complementary to the 25% of a sequence that is not complementary to YB-1 or its cold shock domain to modulate apoptosis.

7. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

8. MPEP 2163 states in part, "An adequate written description of a chemical invention also requires a precise definition, such as by structure, formula, chemical name, or physical properties, and not merely a wish or plan for obtaining the chemical invention claimed. See, e.g., *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004) (The patent at issue claimed a method of selectively inhibiting PGHS-2 activity by administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product, however the patent did not disclose any compounds that can be used in the claimed methods. While there was a description of assays for screening compounds to identify those that inhibit the expression or activity of the PGHS-2 gene product, there was no disclosure of which peptides, polynucleotides, and small organic molecules selectively inhibit PGHS-2. The

court held that "[w]ithout such disclosure, the claimed methods cannot be said to have been described.")."

9. With the exception of the antisense sequences described in the specification, the skilled artisan cannot envision the detailed structure of the encompassed sequences that are antisense to YB-1, the cold shock domain of this protein and sequences having 75% or more identity to these two proteins including those sequences that are complementary to the 25% of a sequence that has no complementarity with YB-1, regardless of the complexity or simplicity of the method of isolation. The skilled artisan cannot envision the detailed structure of an antisense sequence that would have the function of being effective in modulating apoptosis by binding to YB-1, the cold shock domain of this protein and sequences having 75% or more identity to these two proteins, how to deliver an antisense sequence to any organism in an amount and via a delivery method that would allow the nucleic acid to reach the proper cells in an amount that would result in a significant modulation of apoptosis sufficient to alleviate a disease state. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

10. Therefore, only the disclosed antisense sequences, but neither the full breadth of the claimed genus of antisense oligonucleotides directed against YB-1, the cold shock

domain of this protein and sequences having 75% or more identity to these two proteins, including those sequences that are complementary to the 25% of a sequence that has no complementarity with YB-1, that function to modulate apoptosis nor the claimed method of treating any organism other than mice with antisense or decoy oligonucleotides that bind YB-1, the cold shock domain of this protein and sequences having 75% or more identity to these two proteins and modulate apoptosis in a cell meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not fully representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

11. Claim 6 encompasses modulation of apoptosis via mechanisms other than antisense and decoy oligonucleotides. There is no description of any of the other ways of modulating apoptosis that are encompassed by the claimed methods.

Claims 6, 9-11, 14-16 and 24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for increasing apoptotic cell death *in vitro* and *ex vivo* in cell culture and *in vivo* in the mouse, does not reasonably provide enablement for increasing apoptotic cell death by reducing the amount of a transcriptional regulator of apoptosis available to bind to a target polynucleotide *in vivo* in any other organism. Moreover, the specification does not reasonably provide enablement for a method for treating a disease or infection in an organism. The

specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The following factors as enumerated *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), are considered when making a determination that a disclosure is not enabling: the breadth of the claims, the nature of the invention, the state of the prior art, the level of ordinary skill in the art, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples and the quantity of experimentation needed to make the invention based on the content of the disclosure.

12. Claims 6-11, 14-16 and 24 are drawn to methods of increasing apoptotic cell death in a population of cells by reducing the amount of a transcriptional regulator of apoptosis (hereafter referred to as TRA) available to bind to a target polynucleotide. The TRA is defined to be the human Y-box 1 protein, the cold shock domain of this protein and sequences having 75% or more identity to these two proteins. Additional limitations recited include the use of the claimed method to increase apoptotic cell death in tumor cells, the use of antisense or decoy oligonucleotides to reduce the amount of the TRA available to bind the target polynucleotide and the use of the claimed method to increase expression of p53. The method as claimed encompasses use *ex vivo* in cell culture and *in vivo* in all organisms. The methods as claimed also encompass use of the method to treat disease, as evidenced by claim 10, which is drawn to the use of the claimed method in tumor cells.

13. The specification teaches on page 1-2 that regulation of apoptosis has important therapeutic applications against diseases such as Alzheimer's, Parkinson's and multiple sclerosis; ischemic conditions such as heart attack and stroke and even against viral infections such as HIV. Delivery methods for therapeutic nucleic acids are contemplated on pages 14 and 15. The specification teaches in example 2 (pages 26-29) use of antisense and decoy oligonucleotides to modulate the binding of YB-1 and Pur-α to the CD95 promoter and thus modulate apoptosis in HepG2 (liver carcinoma) cells. In example 4 (pages 30-33) antisense and decoy oligonucleotides of YB-1 were also shown to modulate apoptosis by activating p53 in several human cancer cell lines. Example 3 (page 30) describes one *in vivo* use of antisense and decoy oligonucleotides targeted against YB-1 to modulate apoptosis in mice.

14. The state of the prior art is such that use of nucleic acids to modulate cellular processes *in vitro* or *ex vivo* in cell culture is well-known, but use of nucleic acids *in vivo* as therapeutic agents at the time of filing and even to the present time is not routine for several reasons, including the problems of delivery, specificity and duration.

15. The problems of nucleic acid based therapies and antisense technology are well known in the art, particularly with regard to the inability to specifically deliver an effective concentration of a nucleic acid to a target cell, such that a target gene is inhibited to a degree necessary to result in a therapeutic effect. For example, at the time the instant invention was made, the therapeutic use of nucleic acids was a highly unpredictable art due to obstacles that continue to hinder the therapeutic application of nucleic acids *in vivo* (whole organism) (see for example Agrawal et al. (Molecular Medicine Today,

2000, vol 6, p 72-81), Branch (TIBS 1998, vol. 23, p. 45-50) and Jen et al. (Stem Cells 2000, Vol. 18, p 307-319)). Such obstacles include, for example, problems with delivery, target accessibility and the potential for unpredictable nonspecific effects.

16. Jen et al. state (see page 313, second column, second paragraph) "One of the major limitations for the therapeutic use of AS-ODNS and ribozymes is the problem of delivery....presently, some success has been achieved in tissue culture, but efficient delivery for *in vivo* animal studies remains questionable". Jen et al. outlines many of the factors limiting the application of antisense for therapeutic purposes and concludes (see p 315, second column), "Given the state of the art, it is perhaps not surprising that effective and efficient clinical translation of the antisense strategy has proven elusive."

17. Opalinska et al. (Nature Review, 2002, vol 1, p. 503-514) state "[I]t is widely appreciated that the ability of nucleic-acid molecules to modify gene expression *in vivo* is quite variable, and therefore wanting in terms of reliability. Several issues have been implicated as a root cause of this problem, including molecule delivery to targeted cells and specific compartments within cells and identification of sequence that is accessible to hybridization in the genomic DNA or RNA" and in column 2 of the same page, "Another problem in this field is the limited ability to deliver nucleic acids into cells and have them reach their target. Without this ability, it is clear that even an appropriately targeted sequence is not likely to be efficient. As a general rule, oligonucleotides are taken up primarily through a combination of adsorptive and fluid-phase endocytosis. After internalization, confocal and electron microscopy studies have indicated that the

bulk of the oligonucleotides enter the endosome-lysosome compartment, in which most of the material becomes either trapped or degraded."

18. Given this unpredictability, the skilled artisan would require specific guidance to practice the claimed methods *in vivo* in all organisms, with a resultant modulation of apoptosis as claimed. The specification provides examples of modulation of apoptosis by targeting of YB-1 in several cell lines, including human cell lines, however, cell culture examples are generally not predictive of *in vivo* inhibition and the methods of delivery of the exemplified cell line would not be applicable to delivery of oligonucleotides to any organism. Often formulations and techniques for delivery *in vitro* (cell culture) are not applicable *in vivo* (whole organism) (see for example Jen et al., page 313, second column, second paragraph). For example, Agrawal et al. (see p 79-80, section entitled "Cellular uptake facilitators for *in vitro* studies") states "The cellular uptake of negatively charged oligonucleotides is one of the important factors in determining the efficacy of antisense oligonucleotides.....*In vitro*, cellular uptake of antisense oligonucleotides depends on many factors, including cell type, kinetics of uptake, tissue culture conditions, and chemical nature, length and sequence of the oligonucleotide. Any one of these factors can influence the biological activity of an antisense oligonucleotide." Due to differences in the physiological conditions of a cell *in vitro* versus *in vivo*, the uptake and biological activity observed *in vitro* would not predictably translate to *in vivo* results. The specification provides one example of antisense and decoy oligonucleotides to YB-1 being delivered to mice via injection, but this example is not predictive of efficacy in any other organism, including humans.

19. Given these teachings, the skilled artisan would not know *a priori* whether introduction of antisense or decoy oligonucleotides *in vivo* by the broadly disclosed methodologies of the instant invention, would result in successful modulation of apoptosis by reducing the amount of a TRA available to bind a target polynucleotide. One of skill in the art would not know how to deliver oligonucleotides to an organism in such a way that would ensure an amount sufficient to modulate apoptosis is delivered to the proper cell.

20. In fact, the state of the art is such that successful delivery of oligonucleotide sequences *in vivo* or *in vitro*, such that the polynucleotide or oligonucleotide provides the requisite biological effect to the target cells/tissues/organs, must be determined empirically. Methods of inhibiting gene expression using nucleic acids *in vivo* are unpredictable with respect to delivery of the nucleic acid molecule such that the nucleic acid molecule is targeted to the appropriate cell/organ, at a bioeffective concentration and for a period of time such that the nucleic acid molecule is effective in, as in the instant application, attenuating or inhibiting expression of a target gene such that the organism exhibits a loss of function phenotype.

21. The specification does not provide the guidance required to overcome the art-recognized unpredictability of using antisense or decoy oligonucleotides in therapeutic applications in any organism. The field of nucleic acid therapeutics does not provide that guidance, such that the skilled artisan would be able to practice the claimed therapeutic methods.

22. Thus, while the specification is enabling for the examples set forth in the specification, the specification is not enabling for the broad claims of modulating apoptosis in all organisms as the art of introducing nucleic acids into an organism for therapeutic applications is neither routine nor predictable. In order to practice the claimed invention *in vivo* in all organisms a number of variables would have to be optimized, including 1). determining what sequences would constitute antisense sequences capable of binding to YB-1 and what antisense sequences would actually bind to YB-1 and form a strong enough complex that they would be effective at modulating apoptosis, 2). the form of the antisense or decoy oligonucleotide, whether to use a modified oligonucleotide with one or more backbone, sugar or base modifications, 3). the mode of delivery of the antisense or decoy oligonucleotide to an organism that would allow it to reach the targeted cell, 4). the amount of antisense or decoy oligonucleotide that would need to be delivered in order to bind a sufficient amount of YB1 to modulate apoptosis once it reached the proper cell and 5). ensuring the antisense or decoy oligonucleotide remains viable in a cell for a period of time that allows modulation of apoptosis to an extent that there is a measurable and significant therapeutic effect. Each one of these variables would have to be empirically determined for each antisense or decoy oligonucleotide. While optimization of any single one of these steps may be routine, when taken together the amount of experimentation required becomes such that one of skill in the art could not practice the invention commensurate in scope with the claims without undue, trial and error experimentation and therefore, claims 6, 9-11, 14-16 and 24 are not enabled.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 6, 9, 11 and 24 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Wada et al. (Journal of Biological Chemistry, 1995, vol 270, pages 18007-18012, cited on IDS).

Claim 6 is drawn to a method of increasing apoptotic cell death in a population of cells by reducing the amount of a transcriptional regulator of apoptosis available to bind to a target polynucleotide. The TRA is defined to be the human Y-box 1 protein, the cold shock domain of this protein and sequences having 75% or more identity to these two proteins. Claim 9 limits claim 6 by stating the cells are tumor cells. Claim 11 limits claim 6 by stating that method is carried out by contacting the cells with a decoy oligonucleotide comprising a transcriptional regulator of apoptosis binding site. There is no description in the specification that limits a decoy oligonucleotide to a minimum or maximum size or defines whether decoy oligonucleotides are single stranded, double stranded, or both. The only requirement of a decoy oligonucleotide is that it contains a binding site for a TRA. Claim 24 limits claim 11 by stating that the decoy oligonucleotide comprises SEQ ID NO: 2 or SEQ ID NO: 11.

23. Wada et al. disclose the 5' end region of the human *FAS* gene. The disclosed 5' end region contains the sequence shown in SEQ ID NO: 2. (see figure 2 on page 18009, nucleotides -689 to -669) Wada et al. fused this gene region to the coding sequence of luciferase and introduced it into HeLa cells. See page 18009 under section entitled "Stimulation of Fas Promoter Activity by Influenza Virus Infection"

24. Furthermore, since the prior art oligonucleotides meet all the structural limitations of the claims, the prior art oligonucleotides, when introduced into a cell, would then be considered to "reduce the amount of a transcriptional regulator of apoptosis available to bind to a target polynucleotide" as claimed, absent evidence to the contrary. See, for example, MPEP 2112, which states "[w]here applicant claims a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 USC 102 and 103, expressed as a 102/103 rejection. 'There is nothing inconsistent in concurrent rejections for obviousness under 35 USC 103 and for anticipation under 35 USC 102' *In re Best*, 562 F.2d 1252, 1255 n.4, 195 USPQ 430, 433 n.4 (CCPA 1977). This same rationale should also apply to product, apparatus, and process claims claimed in terms of function, property or characteristic. Therefore, a 35 USC 102/103 rejection is appropriate for these types of claims as well as for composition claims."

25. Thus, Wada et al. disclose the method of claim 6 and all the limitations of claims 9, 11 and 24.

Claims 6, 9 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Ohga et al. (Cancer Research, 1996, vol 56, pages 4224-4228).

26. Claim 6 is drawn to a method of increasing apoptotic cell death in a population of cells by reducing the amount of a transcriptional regulator of apoptosis available to bind to a target polynucleotide. The TRA is defined to be the human Y-box 1 protein, the cold shock domain of this protein and sequences having 75% or more identity to these two proteins. Claim 9 limits claim 6 by stating the cells are tumor cells. Claim 10 limits claim 6 by stating the method is performed by contacting the cells with an antisense oligonucleotide targeted to the TRA.

27. Ohga et al. disclose that KB cells (a tumor cell line) that are transfected with an expression vector containing a sequence that is antisense to YB-1 have a reduced level of the YB-1 protein. (see abstract and p. 4226, second column, under heading "Expression of YB-1 Antisense RNA and Drug Sensitivity") Thus, they have reduced amount of the TRA YB-1 in a tumor cell with an antisense oligonucleotide. Ohga et al. do not disclose that apoptosis has been increased in these cells, but as they disclose all the steps of the method of claim 6, it would be inherent in the cells of Ohga et al. that apoptosis is increased.

28. Thus, Ohga et al. disclose the method of claim 6 and all limitations of claims 9 and 10.

Conclusion

Claims 14-16 are free of the prior art searched.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tracy Vivlemore whose telephone number is 571-272-2914. The examiner can normally be reached on Mon-Fri 8:45-5:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file

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Tracy Vivlemore
Examiner
Art Unit 1635

TV
September 21, 2004

SEAN McGARRY
PRIMARY EXAMINER
1635